REMARKS

The presently claimed invention features nucleic acid molecules related to the *S. typhimurium* sspB, sspC, sspD, sspA, sspH, and stpA genes. These genes are important for mediating the uptake of *S. typhimurium* by epithelial cells. The claimed nucleic acid molecules and the proteins they encode are useful for detection of *S. typhimurium* (e.g., for diagnostic purposes) and for producing vaccines. They are also useful in mediating bacterial-mediated endocytosis (e.g., see Example 2 at pages 43-55 of the specification). The molecules can also be used to translocate a second molecule, such as a polypeptide into the cytoplasm of a cell. This approach can be useful for, e.g., the induction or priming of cytotoxic lymphocytes (CTL) directed against the second molecule.

Support for the amendment to the specification at page 18, lines 26-27 is provided at page 2, line 32-page 3, line 1. Support for the amendment to the specification at page 18, lines 28-29 is provided at page 2, line 32-page 3, line 1.

Claims 17-18 and 46-95 are pending. Claims 46-50, 52-56, 58-62, 64-68, 70-74, 76-80, and 82-85 have been amended. Support for the amendments to these claims is found throughout the specification, e.g., at page 10, lines 1-11 (for the term "substantially pure"). No new matter is added by the amendments. Support for new claims 87-95 is found throughout the specification, e.g., at page 51, line 29-page 52, line 25 (claims 88 and 89) and page 43, line 32-page 44, line 4 (claim 91). New claims 87, 90, 92, 93, 94, and 95 are supported, e.g., by Figs. 19, 28, 24, 20, 21, and 26, respectively.

35 U.S.C. § 112, First Paragraph

The Office Action states that "[r]ejection of claims 46-86 and 17-18 under 35 U.S.C. 112, first paragraph is maintained as set forth in the previous office action (Paper No. # 18). Applicants note that the § 112, first paragraph rejection in paper no. 18 was for alleged lack of written description, the present rejection appears to be for both alleged lack of written description (see Office Action at page 2, (third paragraph under item 5), and for alleged lack of enablement (see Office Action at page 4, first full paragraph, "One of skill in the art would

reasonably conclude that the disclosure [sic] fails to provide a representative number of species to describe and enable the genus as broadly claimed"). Because the Office Action refers to paper no. 18, applicant has responded to an alleged lack or written description rejection.

The Office Action states that "[t]he specification discloses an isolated cDNA sequence..." (Office Action at page 2, last paragraph). Applicants do not agree with this characterization. cDNA refers to molecules synthesized by copying RNA into DNA. As discussed in the Response to Office Action filed February 16, 2001, the claimed sequences were cloned and sequenced without producing cDNA.

The Office Action states that "[A]bsent evidence to the contrary, each of the SEQ ID NOS elected for examination is deemed to be an incomplete cDNA" (Office Action at page 2, item 5c). This is discussed below for each group of claims.

Claims 52-63

Applicant respectfully submits that the Office Action's assertion that the nucleic acids are incomplete sequences is unwarranted with respect to claims 52-63 in view of the specification. Independent claims 52 and 58 are drawn to isolated nucleic acid molecules that hybridize under stringent conditions to SEQ ID NO:2 and SEQ ID NO:3, respectively. These sequences are full-length sequences. Simlarly, claims 53 and 59 are drawn to isolated nucleic acid molecules that encode polypeptides comprising SEQ ID NO:6 and SEQ ID NO:7, respectively. These polypeptide sequences are predicted from SEQ ID NO:2 and SEQ ID NO:3.

SEQ ID NO:2 provides the full length coding sequence for the SspC polypeptide (SEQ ID NO:5), and SEQ ID NO:3 provides the full length coding sequence for the SspD polypeptide (SEQ ID NO:7). It is apparent from the specification that the genes encoding SspC and SspD encode full-length polypeptides. For example, the description of Fig. 9 at page 15, lines 26-27 states "[a]n asterisk (*) indicates partially sequenced genes." The sspB and sspA loci are marked with an asterisk but the sspC and sspD loci are not. Furthermore, the specification states "Two complete and two partial open reading frames (ORFs), positioned in the same transcriptional direction, were identified (Fig.9)." (Specification at page 50, lines 12-14). These complete ORFs are identified as sspC and sspD.

The Office Action also alleges that "[t]he instant disclosure of a single species of nucleic acid does not adequately describe the scope of the claimed genus," and quotes *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997) (*U.C. v. Lilly)* "[a] description of a genus of cDNAs may be achieved by means of a recitation of ...structural features common to members of the genus, which features constitutes a substantial portion of the genus." Applicant points out that unlike the claims in *U.C. v. Lilly*, pending claims 52 and 58 require that the claimed nucleic acid molecule hybridize to SEQ ID NO:2 or SEQ ID NO:3 under stringent conditions. The ability to hybridize under specified hybridization conditions to a nucleic acid molecule having a specified sequence is nothing less than a physical property of the claimed molecule. The Court of Appeals for the Federal Circuit has held "[a]n adequate written description of a DNA ...'requires a precise definition, such as by structure, formula, chemical name, or physical properties.'" (*U.C. v. Lilly* 119 F.3d 1559, 1566 (Fed. Cir. 1997)). Because the claimed nucleic acid molecules are defined by a physical property (i.e., hybridization under stringent conditions to a specified sequence), the claims meet the written description requirement as articulated in *U.C. v. Lilly*. Therefore, applicant submits that the rejection for alleged lack of written description should be withdrawn.

Regarding the Office Action's discussion of regulatory sequences (Office Action at pages 3-4), applicant does not see the relevance of this discussion. Identification of such sequences is not a requirement for the written description of a substantially pure nucleic acid molecule as in the present claims. Furthermore, applicant has demonstrated that using information provided by the specification and what is known in the art, sequences of the invention can be incorporated into plasmids, express protein, and can be functional. For example, plasmids constructed as described at page 44, lines 14-25 contained *ssp*CDA (pCH002), *ssp*C (pCH004), *ssp*CD (pCH005), and *ssp*D (pCH006). These plasmids were effective in complementation studies (pCH005, pCH002) and in reconstituting proteins missing in mutants (pCH004 and pCH006) (specification at page 51, line 29-page 52, line 14).

In addition, the Written Description Guidelines make is clear that full length sequences meet the written description requirement. This is made explicit in Example 8 of the Written Description Guidelines ("DNA fragment Encoding a Full Open Reading Frame (ORF)") which discusses the example of a claim drawn to "an isolated and purified nucleic acid comprising" a

sequence containing an open reading frame. The Written Description Guidelines (Example 8) state:

> Weighing all factors including (1) that the full length ORF [of the claimed sequence] is disclosed and (2) that any substantial variability within the genus arises due to addition of elements that are not part of the inventor's particular contribution, taken in view of the level of knowledge and skill in the art, one skilled in the art would recognize from the disclosure that the applicant was in possession of the genus of DNAs that comprise [the claimed sequence].
>
> **Conclusion**: The written description requirement is satisfied.

Claims 52-63 meet the meet the written description requirements described since these claims are defined by their sequences.

Thus, there is no evidence that the additional information regarding regulatory sequences that is apparently required by the Office Action is necessary.

In view of the above discussion, applicants submit that claims 52, 53, 54, 58, 59, and 60 meet the requirements of § 112, first paragraph, as do claims 55-56, 61-63, 17, and 18, which depend from the independent claims.

Claims 46-51

Claim 46 is drawn to an isolated nucleic acid molecule that hybridizes under stringent hybridization conditions to SEQ ID NO:1 (*sspB*). Claim 47 is drawn to an isolated nucleic acid molecule that encodes the amino acid sequence of SEQ ID NO:5 (SspB). Claims 48-50 depend from these claims. The specification states that the SspB sequence is an incomplete protein sequence. However, as discussed above, the stringent hybridization conditions of claim 46 provide a physical characteristic of the claimed nucleic acid. Therefore, claim 46 (and those claims that depend from it) meet the written description requirement under *U.C. v. Lilly*.

Claim 47 specifies a polypeptide sequence and claims a nucleic acid sequence encoding the polypeptide, i.e., degenerate variants of the nucleic acid sequence encoding the polypeptide. The Office Action cites *U.C. v. Lilly* as justification for requiring "definitive or functional features of the claimed genus of polynucleotides" (Office Action at page 3). One of ordinary

skill in the art would garner sufficient information from the polypeptide sequence to make the claimed nucleic acid sequences. This is because one of ordinary skill in the art can generate nucleic acid sequences that will encode the polypeptide using ordinary knowledge. In other words, sufficient structural information is provided such that, when combined with the knowledge of one of ordinary skill in the art, the claimed sequences are adequately described. Thus, the written description requirement is met for claim 47.

Claims 64-69

Claim 64 is drawn to an isolated nucleic acid molecule that hybridizes under stringent hybridization conditions to SEQ ID NO:4 (*sspA*). Claim 65 is drawn to an isolated nucleic acid molecule that encodes the amino acid sequence of SEQ ID NO:8 (SspA). Claims 66-69 depend from these claims. The specification states that the *ssp*A sequence encodes an incomplete protein sequence. As discussed above, the stringent hybridization conditions provide a physical characteristic of the claimed nucleic acid. Therefore, claim 64 (and those claims that depend from it) meet the written description requirement under *U.C. v. Lilly*.

Claim 65 specifies a polypeptide sequence and claims a nucleic acid sequence encoding the polypeptide, i.e., degenerate variants of the nucleic acid sequence encoding the polypeptide. The Office Action cites U.C. v. Lilly as justification for requiring "definitive or functional features of the claimed genus of polynucleotides" (Office Action at page 3). One of ordinary skill in the art would garner sufficient information from the polypeptide sequence to make the claimed nucleic acid sequences. This is because one of ordinary skill in the art can generate nucleic acid sequences that will encode the polypeptide using ordinary knowledge. In other words, sufficient structural information is provided such that, when combined with the knowledge of one of ordinary skill in the art, the claimed sequences are adequately described. Thus, the written description requirement is met for claim 65.

Claims 70-75

Claim 70 is drawn to a substantially pure nucleic acid molecule that hybridizes under stringent conditions to SEQ ID NO:13 (*ssp*H). Claim 71 is drawn to an isolated nucleic acid molecule that encodes the amino acid sequence of SEQ ID NO:14 (SspH). Claims 72-75 depend

from these claims. SEQ ID NO:13 encodes a complete polypeptide sequence encodes a complete polypeptide sequence whose predicted amino acid sequence is provided as SEQ ID NO:14. As discussed above, the stringent hybridization conditions provide a physical characteristic of the claimed nucleic acid. Therefore, claim 70 (and those claims that depend from it) meet the written description requirement under *U.C. v. Lilly*.

Claim 71 specifies a polypeptide sequence and claims a nucleic acid sequence encoding the polypeptide, i.e., degenerate variants of the nucleic acid sequence encoding the polypeptide. The Office Action cites *U.C. v. Lilly* as justification for requiring "definitive or functional features of the claimed genus of polynucleotides" (Office Action at page 3). One of ordinary skill in the art would garner sufficient information from the polypeptide sequence to make the claimed nucleic acid sequences. This is because one of ordinary skill in the art can generate nucleic acid sequences that will encode the polypeptide using ordinary knowledge. In other words, sufficient structural information is provided such that, when combined with the knowledge of one of ordinary skill in the art, the claimed sequences are adequately described. Thus, the written description requirement is met for claim 71.

Claims 76-81

Claim 76 is drawn to a substantially pure nucleic acid molecule that hybridizes under stringent conditions to SEQ ID NO:10 (*stpA*). Claim 77 is drawn to an isolated nucleic acid molecule that encodes the amino acid sequence of SEQ ID NO:12. Claims 78-81 depend from these claims. As discussed above, the stringent hybridization conditions of claim 76 provide a physical characteristic of the claimed nucleic acid. Therefore, claim 76 (and those claims that depend from it) meet the written description requirement under *U.C. v. Lilly*.

Claim 77 specifies a polypeptide sequence and claims a nucleic acid sequence encoding the polypeptide, i.e., degenerate variants of the nucleic acid sequence encoding the polypeptide. The Office Action cites U.C. v. Lilly as justification for requiring "definitive or functional features of the claimed genus of polynucleotides" (Office Action at page 3). One of ordinary skill in the art would garner sufficient information from the polypeptide sequence to make the claimed nucleic acid sequences. This is because one of ordinary skill in the art can generate nucleic acid sequences that will encode the polypeptide using ordinary knowledge. In other

words, sufficient structural information is provided such that, when combined with the knowledge of one of ordinary skill in the art, the claimed sequences are adequately described. Thus, the written description requirement is met for claim 77.

Claims 82-86

Claim 82 is drawn to a substantially pure nucleic acid molecule that hybridizes under stringent conditions to SEQ ID NO:15 which contains sequence encoding SspA, Ssp B, SspC, and SspD. SEQ ID NO:15 contains two complete sequences (i.e., those encoding SspC and SspD). Therefore, the Office Action is incorrect in its presumption that the sequence is incomplete. Furthermore, the stringent hybridization conditions of claim 82 provide a physical characteristic of the claimed nucleic acid. Therefore, claim 82 (and those claims that depend from it-claims 83-86) meet the written description requirement under *U.C. v. Lilly.*

35 U.S.C. § 102 (a)

Claims 46-86 are rejected as allegedly anticipated by WO 95/02048 ('048). Claims 46-86 and 17-18 are rejected as allegedly anticipated by Hermant et al. and Kaniga et al. Each reference is discussed separately below.

WO 95/02048 (the '048 application)

The Office Action states that the '048 application was cited against the present application "because the claims as recited broadly could read on DNA of *S. typhi* which contain SspB, SspC, SspD, and SspA genes." Applicant points out that all of the independent pending claims drawn to a nucleic acid are drawn to a substantially pure nucleic acid molecule. The definition of a substantially pure nucleic acid is provided in the specification at page 10, lines 1-7;

> A substantially pure DNA, as used herein, refers to a nucleic acid sequence, segment, or fragment, which has been purified from the sequences which flank it in a naturally occurring state, e.g., a DNA which has been removed from the sequences which are normally

> adjacent to the fragment, e.g., the sequences adjacent to the fragment in the genome in which it naturally occurs.

This definition makes it clear that the claimed nucleic acids are removed from naturally occurring flanking sequence, thus, the claims do not read on the naturally occurring DNA in a *Salmonella* cell. Thus, the present claims are not anticipated by the '048 application.

The Office Action also states "[i]n the absence of evidence to the contrary, the disclosed prior art bacterial cell comprises the nucleic acid molecules...as recited in the claims" (Office Action at page 4). As discussed above, the claims are drawn to "substantially pure" nucleic acid molecules. There is no evidence that the reference discloses any of the claimed isolated nucleic acid molecules. Some of the pending claims are drawn to a host cell containing an isolated nucleic acid molecule or a vector comprising an isolated nucleic acid molecule (claims 49, 50, 56, 57, 62, 63, 68, 69, 74, 75, 80, 81, 85, and 86). There is no evidence that any of the cells disclosed in '048 contain such isolated nucleic acid molecules or the claimed vectors. Therefore, the reference cannot anticipate the claimed invention and applicant respectfully requests that the rejection under 35 U.S.C. § 102 (a) be withdrawn.

Hermant et al.

The Office Action states that "Exhibit D," a date stamped page of the journal in which Hermant was published (October 3, 1995) that was filed with the February 16, 2001, Response was not sufficient to overcome the rejection because the reference (Hermant) was made available to the public prior to the filing date of the priority application (November 14, 1995). The Office Action also states that Exhibit C contained conclusory statements without sufficient evidentiary support. The Declaration states that the pages provided with Exhibit C have a date prior to the October 3, 1995 date of Hermant et al. The Office Action states that "[e]videntiary support may include copies of pertinent lab note book entries..." This is what was provided in Exhibit C. The pages are printouts of a sequence analysis conducted prior to October 3, 1995. The pages were prepared as part of routine record keeping prior to October 3, 1995, as evidenced by the Declaration. The applicant has provided appropriate supporting evidence (in Exhibit C) demonstrating that

> Prior to July 8, 1995, sequencing of the open reading frames produced the sequence in the attached document which was prepared prior to July 8, 1995.

The supporting evidence was in the form of contemporaneous documents that are pertinent laboratory notebook entries. The Examiner is not free to simply dismiss this evidence. It is unclear to the applicant what more the Examiner requires.

In view of the above discussion, applicant submits that Hermant does not anticipate the present invention and therefore requests that the rejection under 35 U.S.C. § 102 (a) in view of Hermant be withdrawn.

Kaniga et al.

Applicants assume that this is a rejection even though the Office Action states "in view of applicants [sic] submission of evidence "exhibit B and C" Examiner has withdrawn" since the Office Action goes on to provide additional detail about a rejection. As discussed above, Exhibit C, provided with the Response filed on February 16, 2001, provided evidence in the form of notebook pages dated prior to the publication date of Kaniga, that "sequencing of the open reading frames produced the sequence in the attached document which was prepared prior to July 8, 1995." The Office Action states that "[e]videntiary support may include copies of pertinent lab note book entries" (Office Action at pag. 5). As discussed above, this is what applicant provided in Exhibit C. Applicant does not believe that additional evidence is necessary. If the examiner believes that additional evidence is required, applicant respectfully requests that specific instruction be provided regarding the perceived deficiencies of Exhibit C.

Thus, it is clear that Kaniga's amino acid sequences cannot anticipate any of the nucleic acid sequences of the present invention including SspB and SspC. In view of the arguments presented above, applicants respectfully request withdrawal of the rejection in view of Kaniga et al. under 35 U.S.C. § 102 (a).

CONCLUSION

Attached is a marked-up version of the changes being made by the current amendment.

Applicant submits that all of the claims are in condition for allowance, which action is requested. Enclosed is a Petition for Extension of Time with the required fee. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing attorney docket no. 00786-292002.

Respectfully submitted,

Date: November 8, 2001

for Anita Meiklejohn
Reg. No. 35,283

Jeffrey D. Hsi
Reg. No. 40,024

Fish & Richardson P.C.
225 Franklin Street
Boston, Massachusetts 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906

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Version with markings to show changes made

In the specification

Replace the paragraph at page 18, lines 26-27 with the following paragraph:

Fig. 26 is a depiction of the nucleic acid sequence of [prgH] sspH (SEQ ID NO: 13).

Replace the paragraph at page 18, lines 28-29 with the following paragraph:

Fig. 27 is a depiction of the predicted amino acid [sequences] sequence of [prgB] SspH (SEQ ID NO: 14).

In the claims:

Claim numbers 87-95 are new:

87. (New) An substantially pure nucleic acid consisting essentially of SEQ ID NO:1.

88. (New) The substantially pure nucleic acid molecule of claim 52 or claim 53, wherein the polypeptide encoded by the substantially pure nucleic acid molecule can induce bacterial-mediated endocytosis (BME) in the absence of a wild type SspC polypeptide.

89. (New) The substantially pure nucleic acid molecule of claim 58 or claim 59, wherein the polypeptide encoded by the nucleic acid molecule can induce bacterial-mediated endocytosis (BME) in the absence of a wild type SspD polypeptide.

90. (New) A substantially pure nucleic acid molecule consisting essentially of SEQ ID NO:4.

91. (New) The substantially pure nucleic acid molecule of claim 64 or 65, wherein the polypeptide encoded by the nucleic acid molecule can induce bacterial-mediated endocytosis (BME) in the absence of a wild type SspA polypeptide.

92. (New) A substantially pure nucleic acid molecule consisting essentially of SEQ ID NO:10.

93. (New) A substantially pure nucleic acid molecule consisting essentially of SEQ ID NO:2

94. (New) A substantially pure nucleic acid molecule consisting essentially of SEQ ID NO:3.

95. (New) A substantially pure nucleic acid molecule consisting essentially of SEQ ID NO:13.

Claims 46-50, 52-56, 58-62, 64-68, 70-74, 77-80, and 82-85 have been amended as follows (all of the claims are provided for the convenience of the examiner):

17. (Amended) A method of inducing uptake of a bacterial cell by an epithelial cell in a mammal, comprising increasing expression of the nucleic acid molecule of claim 46 or 52 in said bacterial cell and administering said bacterial cell to said mammal.

18. The method of claim 17, wherein said bacterial cell is a Salmonella cell.

46. (Amended twice) [An isolated] A substantially pure nucleic acid molecule which hybridizes under conditions of hybridization in 50% formamide at 42°C and washing in 0.1 X SSC at 65°C to a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO:1.

47. (Amended) [An isolated] A substantially pure nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 5.

48. (Amended) The [isolated] substantially pure nucleic acid molecule of claim 47 comprising the nucleotide sequence of SEQ ID NO: 1.

49. (Amended) A vector comprising the [isolated] substantially pure nucleic acid molecule of any of claims 46, 47, or 48.

50. (Amended) A host cell comprising the [isolated] substantially pure nucleic acid molecule of any of claims 46, 47, or 48.

51. A host cell comprising the vector of claim 49.

52. (Amended twice) [An isolated] substantially pure nucleic acid molecule which hybridizes under conditions of hybridization in 50% formamide at 42°C and washing in 0.1 X SSC at 65°C to a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO:2.

53. (Amended) [An isolated] A substantially pure nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:6.

54. (Amended) A [An isolated] substantially pure nucleic acid molecule [of claim 52] comprising the nucleotide sequence of SEQ ID NO: 2.

55. (Amended) A vector comprising the [isolated] substantially pure nucleic acid molecule of any of claims 52, 53, or 54.

56. A host cell comprising the [isolated] substantially pure nucleic acid molecule of any of claims 52, 53, or 54.

57. A host cell comprising the vector of claim 55.

58. (Amended twice) [An isolated] A substantially pure nucleic acid molecule which hybridizes under conditions of hybridization in 50% formamide at 42°C and washing in 0.1 X SSC at 65°C to a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO:3.

59. (Amended) [An isolated] A substantially pure nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:7.

60. (Amended) [The isolated] A substantially pure nucleic acid molecule [of claim 59] comprising the nucleotide sequence of SEQ ID NO: 3.

61. (Amended) A vector comprising the [isolated] substantially pure nucleic acid molecule of any of claims 58, 59, or 60.

62. (Amended) A host cell comprising the [isolated] substantially pure nucleic acid molecule of any of claims 58, 59, or 60.

63. A host cell comprising the vector of claim 61.

64. (Amended twice) [An isolated] substantially pure nucleic acid molecule which hybridizes under conditions of hybridization in 50% formamide at 42°C and washing in 0.1 X SSC at 65°C to a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO:4.

65. (Amended) [An isolated] A substantially pure nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:8.

66. (Amended) The [isolated] substantially pure nucleic acid molecule of claim 65 comprising the nucleotide sequence of SEQ ID NO:4.

67. (Amended) A vector comprising the [isolated] substantially pure nucleic acid molecule of any of claims 64, 65, or 66.

68. (Amended) A host cell comprising the [isolated] substantially pure nucleic acid molecule of any of claims 64, 65, or 66.

69. A host cell comprising the vector of claim 67.

70. (Amended) [An isolated] A substantially pure nucleic acid molecule which hybridizes under conditions of hybridization in 50% formamide at 42°C and washing in 0.1 X SSC at 65°C to a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO:13.

71. (Amended) [An isolated] A substantially pure nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:14.

72. (Amended) [The isolated] A substantially pure nucleic acid molecule [of claim 71] comprising the nucleotide sequence of SEQ ID NO: 13.

73. (Amended) A vector comprising the [isolated] substantially pure nucleic acid molecule of any of claims 70, 71, or 72.

74. (Amended) A host cell comprising the [isolated] substantially pure nucleic acid molecule of any of claims 70, 71, or 72.

75. A host cell comprising the vector of claim 73.

76. (Amended) [An isolated] A substantially pure nucleic acid molecule which hybridizes under conditions of hybridization in 50% formamide at 42°C and washing in 0.1 X SSC at 65°C to a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO:10.

77. (Amended twice) [An isolated] A substantially pure nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 12.

78. (Amended) The [isolated] substantially pure nucleic acid molecule of claim 77 comprising the nucleotide sequence of SEQ ID NO: 10.

79. (Amended) A vector comprising the [isolated] substantially pure nucleic acid molecule of any of claims 76, 77, or 78.

80. (Amended) A host cell comprising the [isolated] substantially pure nucleic acid molecule of any of claims 76, 77, or 78.

81. A host cell comprising the vector of claim 79.

82. (Amended twice) [An isolated] substantially pure nucleic acid molecule which hybridizes under conditions of hybridization in 50% formamide at 42°C and washing in 0.1 X SSC at 65°C to a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO:15.

83. (Amended) The [isolated] substantially pure nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 15.

84. (Amended) A vector comprising the [isolated] substantially pure nucleic acid molecule of any of claims 82 or 83.

85. (Amended) A host cell comprising the [isolated] substantially pure nucleic acid molecule of any of claims 82 or 83.

86. A host cell comprising the vector of claim 84.